Remarks

The present rejections should be reconsidered. A review of the present claims compared to the prior art reveals that the claims should be found to be allowable.

Overview of the Applicant's Invention

In the background section of the patent, the inventor sets out a problem: during electrophoretic separations a specific optimal temperature is preferred to differentiate genetic oligonucleotide variants having conformational differences. In prior methods the separation channel would be exposed to a single temperature gradient during an electrophoresis separation run. The applicant has discovered that by exposing the separation channel to "cycling" temperature gradients (i.e. repeated cycles between a lower and a higher temperature) the sample is more likely to spend more time at the ideal temperature for denaturation and separation of mutant types. In the claimed method, the start of the sample separation requires the presence of a prepared sample (e.g., amplified oligonucleotides). This sample is injected into a separation channel and exposed to temperature cycling while the separation is taking place. Following separation the samples are detected. It is notable that the temperature cycling is not used for amplification of nucleic acid. As will later be shown, such amplification during separation would probably not be possible.

Section 102

The rejection under section 102 should be reconsidered as the cited reference does not teach the elements of the applicant's claims.

A claim is anticipated only if each and every element as set forth in the claim is found in a single cited art reference. See Verdegaal Bros. v. Union Oil of

California, 814 F.2d 628, 2 USPQ2d 1051, 1053 (Fed. Cir. 1987). The identical invention must be shown in as complete detail as is contained in the claim. See Richardson v. Suzuki Motor Co., 868 F.2d 1226, 1236, 9 USPQ2d 1913, 1920 (Fed. Cir. 1989).

One claimed step in the method of claim 1 is not taught in Chow, the cited reference. The claimed method includes the step of "exposing the separation channel to a cycling temperature gradient while electrophoretically separating the sample." Thus, the separation of the sample and the cycling of the temperature take place at the same time. The section from Chow instructs "(white blood cells) were electrophorsed through the cannel to the well containing the PCR reaction mixture until 20-100 lyphocytes were in the PCR well. The entire device was thermally cycled and the DNA separated as for the previous example". The previous example, Example 2, specifies that the electrophoretic separation of the sample and the amplification are separate steps. From this it is apparent that the reference is specifying subsequent steps of electrophoretic transport, thermal cycling, and subsequent DNA separation. Specifically the use of AC Thermal Cycling is used during the amplification "to prevent electroosmotic movement of the amplification mix through the amplification channel". (see col. 38, lines 25-27). Rather than teaching what the applicant has claimed (simultaneous separation and temperature cycling) the cited reference teaches that this should be prevented.

To effect a PCR reaction a reaction mixture is cycled through repeated temperature cycles. This cycle generally includes an melting temperature stage (during which double stranded DNA is separated into single stranded DNA), an annealing temperature stage (a lower temperature to allow the relatively short DNA primers to anneal to target DNA sequences) and an extension temperature stage (during which the polymerase adds bases to the primer, producing amplified

copies of the targeted sequence). This reaction also requires the reaction components, namely: dNTPs, primers, target DNA, a polymerase, and as the reaction progresses amplified copies of a sequence. If separation were occurring during temperature cycling, as suggested, the dNTPs, primers, amplified sequences and target DNA would all begin to separate, migrating at separate rates thereby preventing the interaction of reaction components required for the reaction to take place. The identical claimed invention of the applicant is not shown in the cited reference.

Section 103

The rejections under Section 103 should also be reconsidered because the references fail to teach the claimed method.

An obviousness determination requires determining the scope and content of the prior art and ascertaining the differences between the cited art and the claims at issue. See Graham v. John Deere Co., 148 USPQ 459 (S.C. 1966). When applying 35 USC Section 103 in a finding of obviousness, the tenants of patent law require that the claimed invention be considered as a whole, that the cited references must suggest the desirability and thus the obviousness of making the claimed combination, that the cited references must be viewed without the benefit of impermissible hindsight afforded by the claimed invention, and that the cited reference provide a reasonable expectation of success in practicing the claimed technology. See Hodosh v. Block Drug Co., Inc., 229 USPQ 182, 187 (Fed. Cir. 1986).

On pages 4-6, the Office action finds the applicant's claims unpatentable over Li in view of Chow. However this combination does not render obvious the applicant's claims.

First, the stated legal requirement is that the cited references must contain a teaching to combine the

references. The cited motivation to combine, set out on page 5 of the Office action, was that it would have been obvious "to cycle the temperature gradient in the method of capillary separation of Li because large quantities of DNA variants can be produced from very small quantities of starting materials". The same reason is given for the combination of Mansfield with Chow on page 8 of the Office action. As noted above, the desire to have effective exponential copying of a select sequence is the reason you would not use the separation of Li while also trying to amplify using temperature gradient cycling to effect PCR. The components of the reaction would move apart as each migrates at a separate rate, preventing the combination of reagents. The cited motivation is a powerful reason why the references would not be combined.

Second, even if these two combination of references were made, neither teaches the applicant's claimed steps. With regard to the combination of Li and Chow, the Office action relies on Chow to teach the cycling of temperature during separation. However as already noted, Chow does not teach this step. Instead, this step would thwart the very purpose of the methods discussed by Chow. Chow in fact explicitly teaches away from the claimed step.

With respect to Mansfield in combination with Chow, the specific language of step e of the applicant's claim is not mentioned in the Office action. Again Chow is cited for teaching the cycling of temperature gradients and again this simply does not reach the claimed method. Even if it were possible to amplify during separation, what is specifically claimed in step e is found in neither reference. Step e requires that "a plurality of temperature cycles occur between sample injections". If Chow teaches to amplify DNA using PCR, such an amplification would require similar conditions (i.e., the same number of cycles) for each sample to result in comparable data. However, under the applicant's claimed method earlier injected samples would undergo additional

cycles. There is simply nothing in either reference teaching temperature cycling of multiple cycles between multiple injections, as is claimed.

Conclusion

For the stated reasons, the present rejection should be reconsidered. A notice of allowance is earnestly solicited.

CERTIFICATE OF MAILING

I hereby certify that this paper (along with any paper referred to as being attached or enclosed) is being deposited with the United States Postal Service on the date shown below with sufficient postage as first class mail in an envelope addressed to: Commissioner for Patents, P.O. Box 1450, Alexandria, VA 22313-1450.

Signed: Sally Azevedo
Typed Name: Sally Azevedo

Date: June 23, 2005

Respectfully submitted,

David M. Schneck
Reg. No. 43,094

P.O. Box 2-E
San Jose, CA 95109-0005
(408) 297-9733